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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,019	10/20/2003	Jeremy Nathans	JHU1380-2	5064

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,019	NATHANS ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-40* is/are pending in the application.

4a) Of the above claim(s) *21-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed 3-27-07 has been entered into the record. Claims 19-40 are pending.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Information Disclosure Statement

The information disclosure statement filed 10-20-03 with previous initials from previous applications has not been initialed as considered herein. MPEP 609.02 states: 2. Continuation Applications, Divisional Applications, or Continuation-in-Part Applications Filed Under 37 CFR 1.53(b) The examiner will consider information which has been considered by the Office in a parent application when examining: (A) a continuation application filed under 37 CFR 1.53(b), (B) a divisional application filed under 37 CFR 1.53(b), or (C) a continuation- in-part application filed under 37 CFR 1.53(b). A listing of the information need not be resubmitted in the continuing application unless the applicant desires the information to be printed on the patent. ***If resubmitting a listing of the information, applicant should submit a new listing that complies with the format requirements in 37 CFR 1.98(a)(1). Applicants are strongly discouraged from submitting a list that includes copies of PTO/SB/08 ** or PTO-892 forms from other applications. A completed PTO/SB/08 ** form from another application may already have initials of***

an examiner and the application number of another application. This information will likely confuse the record. Furthermore, when the spaces provided on the form have initials of an examiner, there are no spaces available next to the documents listed for the examiner of the subsequent application to provide his or her initials, and the previously relevant initials may be erroneously construed as being applied for the current application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 19, 20, 38-40 in the response filed 3-27-07is acknowledged. The traversal is on the ground(s) that that search of groups I-III are overlapping in that the antibody is used in the methods of Groups II and III. This is not found persuasive because MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.01). In the instant situation, the inventions of Groups I, II and III are drawn to distinct inventions which are related as separate products capable of separate manufacture, use or sale as described in the previous Office Action. Restrictions between the inventions is deemed to be proper for the reasons previously set forth.

In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. In the instant case a burden has been established in showing that the inventions of Groups II and III are classified separately necessitating different searches of issued U.S. Patents. However, classification of subject matter is merely one

indication of the burdensome nature of search. The literature search, particularly relevant in this art, is not co-extensive, because, for example, methods of treatment require different considerations as compared to methods of detection. Additionally, it is submitted that the inventions of Groups I, II and III have acquired a separate status in the art. Clearly different searches and issues are involved in the examination of each Group.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 21-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3-27-07.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19 and 38-40 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed invention is drawn to a antibody which is a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, purity of naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui 156 USPQ 426 (1966). However when purity results in

new utility, patentability is considered. Merck Co. V. Chase Chemical Co. 273 F. Supp 68 (1967). See also American Wood v. Fiber Disintergrating Co., 90 US 566 (1974); American Fruit Growers v. Brogdex Co. 283 US 1 (1931); Funk Brothers Seed Co. V. Kalo Innoculant Co. 33 US 127 (1948). Filing of arguments and evidence of a new utility imparted by the increased purity of the claimed invention *and amendment to the claims to recite the essential purity* of the claimed products is suggested to obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19, 20 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to antibodies that bind a genus of fibroblast growth factor homologous factor-4 polypeptides or "FHF-4" polypeptides (claim 19, 20 and 40), a genus of FHF-4 polypeptides with the characteristics presented in claim 38 and 39. The specification teaches a FHF-4 polypeptide which is a human polypeptide as set forth in SEQ ID NO:4 and the murine FHF-4 polypeptide as set forth in SEQ ID NO:11. The claims recite no structure or function that defines "FHF-4" from the family of fibroblast growth factors. The specification teaches that the FHF's belong to the family of fibroblast growth factors. The art teaches that teaches that the members of the FGF family are related by structure and function. Greene et al (US Patent no 6,482,408) teaches that each member of the family has functions overlapping with others and also has its unique spectrum of functions (column 1-2). The claims do not recite structural and functional characteristics of the FHF-4 polypeptide genus that define it over the FGF family in general or uniquely characterize the genus of FHF-4 polypeptides. The functional characteristics recited in the claims are shared characteristics of the prior art FGF polypeptide family. The claims and the specification does not place any structure, chemical or functional limitations on the variants of FHF-4 polypeptides. The recitation of "FHF-4" does not convey a common structure or function. The scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Structural and functional features that could distinguish compounds in the genus from others in the FGF-family are missing from the disclosure and the claims. No common structural attributes identify the members of the genus to which the antibody binds. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure fails to describe the common attributes or structural characteristics that identify members of the genus, and because the genus is highly variant, the function of the binding of antibody alone is insufficient to describe the genus of polypeptides of that function equivalently. One of skill in the art

would reasonable conclude that the disclosure of a SEQ ID NO:4 and 11, fails to provide a representative number of species of FHF-4 to describe the claimed genus to which the antibodies bind. Applicants were not in possession of the claimed genus antibodies because the specification does not convey to one of skill in the art a representative number of variants in structure and function of any such polypeptide that has the claimed/structure and function and therefore, lack logically description of the genus of antibodies that bind the genus of FHF-4 polypeptides. The recitation of "FHF-4" does not convey a common structure nor a common function. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant and not conveyed by way of written description by the specification at the time of filing. As such the specification lacks written description for the highly variant genus that has no structure and function and one skilled in the art would not recognize that applicants had possession of the genus of claimed antibodies that bind a genus of structurally and functionally undefined polypeptides that also lack written description.

Furthermore, explicit support for the limitation of claim 39 is not found in the original claims, nor readily apparent in the specification as originally filed. As such, this claim appears to lack conception by way of written description at the time of filing. This issue is best resolved by Applicants pointing to the specification by page and line number where written description of this later claimed invention is apparent.

Claims 19, 20 and 3840 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 19 and dependent claims 20 and 38-40, the term "substantially pure" is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite

degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

As to claim 39, the claim is indefinite because claim 39 does not particularly point out what the at least five consecutive amino acids that are conserved in the amino acids of SEQ ID NO:4 are conserved in the genus of FHF-4 polypeptides.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant

for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 19 and 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Patry et al (FEBS Letters, 349:23-28, 1994).

The claims are drawn to FHF-4 polypeptides and FHF-4 polypeptides characterized as about 225-250 amino acids in length, lacking an amino terminal signal peptide, and containing a nuclear localization signal.

Patry et al. teach high and low molecular weight forms of FGF-2. The FGF-2 protein lacks an amino terminal signal peptide and contains a nuclear localization signal. The forms of FGF-2 of Patry et al. are generated by alternate translational initiation sites and range from 196 to 210 amino acids in length. (See page 23, first column, third paragraph). These proteins appear to meet the description of FHF-4 proteins as characterized in the claims, assuming about 225-250. Consequently, the broad scope of the claims encompassing all variants that encode any FHF-4 protein meeting the definitions of the claims would appear to be anticipated by the reference. Please note that the recitation of FHF-4 in the claims does not convey any structural or functional difference as compared to the FGF-2 of the prior art. Patry et al teach polyclonal antibodies that bind the FGF-2 of the art at page 24, column 1, under Immunoblot

Analysis. The polyclonal antibody of comprises the antigen binding fragment of claim 40. The term "having" is interpreted as open language. As such, the antibody of the prior art meets the limitation of the claims.

Claims 19, 20 and 38-40 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Greene et al (US Patent No. 6,482,408, with priority to June 5, 1995).

Greene et al teach the polypeptide of SEQ ID NO:2. The polypeptide of SEQ ID NO:2 is identified as fibroblast growth factor-15 (FGF-15). Greene et al teach that FGF-15 belongs to the FGF family of structurally related and the FGF/HBGF family signature is conserved in the FGF-15 polypeptide of the present invention (see column 4, lines 27-31). Greene et al claims antibodies or portions thereof that bind SEQ ID NO:2 or fragments consisting of 30 or 50 contiguous amino acids thereof or fragments having cellular growth activity. Greene et al contemplates monoclonal antibodies, polyclonal antibodies, chimeric antibodies, humanized antibodies, single chain antibodies and Fab fragments and compositions comprising such. Given that the polypeptide of the prior art has at least 117 consecutive residues that are identical with SEQ ID NO:4, the claimed antibodies of the prior art would inherently bind SEQ ID NO:4 of FHF-4 which has the properties recited in claims 38 and 39.

Applicants should note that prior invention may not be established under 37 CFR 1.131 because this rejection is based upon a U.S. patent or U.S. patent application publication of a pending or patented application to another or others which claims the same patentable invention as defined in § 41.203(a) of this title, in which case an applicant may suggest an interference pursuant to § 41.202(a) of this title.

Claims 19, 20 and 38-40 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Nathans et al (5,872,226, with priority to May 12, 1995).

The claims are drawn to antibodies that bind FHF-4 polypeptides and FHF-4 polypeptides characterized as about 225-250 amino acids in length, lacking an amino terminal signal peptide, containing a nuclear localization signal .or at least 5 conserved consecutive amino acids of SEQ ID NO:4

Nathans et al, teach SEQ ID NO:2 that is a FHF-1 polypeptide. The FHF-1 protein lacks an apparent amino terminal signal peptide and contains a nuclear localization signal and comprises at least 5 consecutive amino acids from SEQ ID NO:2. The FHF-1 polypeptide of Nathans et al is 243 amino acids in length, and is set forth in SEQ ID NO:2. These proteins appear to meet the description of FHF proteins as characterized in the claims, assuming about 225-250. Please note that the recitation of FHF-4 in the claims does not convey any structural or functional difference as compared to the FHF-1 polypeptide of the prior art. Nathans et al teach antibodies that bind SEQ ID NO:2 and FHF-1 at columns 7-8. Nathans et al specifically teach polyclonal, monoclonal, and antibody fragments such as Fv and Fab. As such, Nathans et al renders the instant claims anticipated.

Claims 19, 20, 38 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Hu et al (U.S. Patent 5,817,485, issued October 6, 1998, with priority to March 8, 1994).

The claims are drawn to FHF-4 polypeptides and FHF-4 polypeptides characterized as about 225-250 amino acids in length, lacking an amino terminal signal peptide, containing a nuclear localization signal.

Hu et al, teach FGF-10. The FGF-10 protein lacks an apparent amino terminal signal peptide and contains a nuclear localization signal and comprises SEQ ID NO:24 (see attached alignment). The FGF-10 polypeptide of Hu et al is 181 amino acids in length, and is set forth in SEQ ID NO:2. This protein meets the description of FHF-4 polypeptides as characterized in the claim 38, assuming about 225-250. Consequently, the broad scope

of the claims encompassing all possible proteins that encode any FHF-4 protein meeting the definitions of the claims would appear to be anticipated by the reference. Please note that the recitation of FHF-4 does not convey any structural or functional difference as compared to the FGF-10 of the prior art. Hu et al teaches polyclonal, monoclonal, chimeric, single chain, humanized antibodies and Fab fragments at column 11, line 42 to column 12, line 13. As such, Hu et al anticipates the instantly claimed invention.

Status of the Claims

Claims 1, 2 and 38-40 stand rejected. Claims 21-37 are withdrawn from consideration.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Examiner Jeffrey Siew can be reached on 571-272-0787.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy, Ph.D.

Primary Examiner

Art Unit 1645